

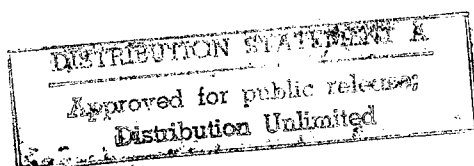
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# ***JPRS Report***

# **Science & Technology**

***Central Eurasia:  
Life Sciences***

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# Science & Technology

## Central Eurasia: Life Sciences

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6 May 1993

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**Synthesis and Properties of Novel DSP Analogs.  
Part 1. Antiepileptic Effects**

937C0195B Moscow *BIOORGANICHESKAYA  
KHIMIYA* in Russian Vol 19 No 1, Jan 93 (manuscript  
received 23 Jul 92) pp 43-55

[Article by I. A. Prudchenko, L. V. Stashevskaya, I. I. Mikhaleva, V. T. Ivanov, A. A. Shandra\*, L. S. Godlevskiy\* and A. M. Mazarati\*, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; \*Odessa Medical Institute imeni N. I. Pirogov; UDC 577.175.82.15: 577.151.7]

[Abstract] A series of novel analogs of DSP (delta sleep peptide) were synthesized by conventional solid-phase technique using Fmoc- and Boc-schemes. The peptides, modified at positions 1, 2 and 6, were then assessed for potential antiepileptic properties in picrotoxin-treated Wistar rats (200-230 g) and pentylenetetrazole-primed BALB/C (18-22 g) mice. Three modified peptides were shown to possess antiepileptic activities on intraperitoneal administration to rats (1.0 mg/kg) and intrahippocampal administration to mice (50 µg/kg). Key factors imparting antiepileptogenic properties to the peptides consisted of replacement of tryptophan-1 by tyrosine and concomitant substitution of proline or D-alanine for alanine-2. In addition replacement of alanine-2 by β-alanine as the sole change was also shown to yield a peptide with enhanced antiepileptogenic activity. Antiepileptogenic activity was in part enhanced by the relative resistance of these peptides to proteolysis and efficiency in permeation through the blood-brain barrier. Figures 5; references 14: 5 Russian, 9 Western.

**Solid-Phase Synthesis of Membrane-Spanning  
Peptides of Bacteriorhodopsin**

937C0195C Moscow *BIOORGANICHESKAYA  
KHIMIYA* in Russian Vol 19 No 1, Jan 93 (manuscript  
received 18 Jun 92) pp 56-65

[Article by L. D. Chikin, A. B. Moshnikova, Zh. O. Grebennikova, A. T. Kozhich and V. T. Ivanov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.112.6: 542.95]

[Abstract] Beckman-990 automatic synthesizer was used for the solid-phase synthesis of the membrane-spanning C, D, E and G peptide fragments of bacteriorhodopsin. Synthesis was facilitated by replacement of methionine residues at positions 68, 118, 145 and 210 by norleucine and was based on conventional Boc technique on PAM polystyrene support. Purification of the peptides was attained by preparative HPLC; <sup>1</sup>H-NMR and analytical HPLC were used to confirm the synthesis of the C (67-106), D (87-136), E (128-162) and G (190-233) peptides. Figures 6; references 13: 4 Russian, 9 Western.

**Diagnostic and Prognostic Significance of Plasma  
Diene Conjugate Levels in Septic Infants**

937C0200A Moscow *KLINICHESKAYA  
LABORATORNAYA DIAGNOSTIKA* in Russian  
No 9-10, Sep-Oct 92 (manuscript received 10 Jul 91)  
pp 15-18

[Article by M. K. Soboleva and V. I. Sharapov, Novosibirsk Medical Institute; UDC 616.94-07:616.153.915-39-074]

[Abstract] Plasma and erythrocyte levels of malonic dialdehyde and diene conjugates—products of lipid peroxidation—were monitored in 52 infants, 1-11 months old, with various septic conditions. The results demonstrated that both factors have diagnostic and prognostic significance, with the diene conjugates proving to be an earlier and a more sensitive indicator. Sepsis correlated with a parallel 2.6- to 3.4-fold rise ( $p < 0.001$ ) in both indicators, followed by abatement and return to baseline levels as the clinical course improved. In terminal cases, however, the levels of the diene conjugates fell significantly ( $p < 0.001$ ) below baseline values. Figures 2; references 10: 7 Russian, 3 Western.

**Myoglobin as Indicator of Human Adaptation and  
Pathology**

937C0200B Moscow *KLINICHESKAYA  
LABORATORNAYA DIAGNOSTIKA* in Russian  
No 9-10, Sep-Oct 92 (manuscript received 06 Aug 91)  
pp 18-21

[Article by A. L. Chernyayev, Laboratory of Geographical Pathology, Scientific Research Institute of Human Morphology, Russian Academy of Medical Sciences, Moscow; UDC 616.153.962.4-074]

[Abstract] Evaluation of serum myoglobin as an indicator of human adaptation and pathology was performed on 342 males aged 20-55. The RIA studies demonstrated that initial adaptation to the climate of Magadan (one month to six years) was accompanied by elevated serum myoglobin (102.4-108.6 ng/ml), followed by decline to above-baseline levels on adaptation to 53.2 ng/ml after 15 years vs. 41.9 ng/ml baseline for Moscow. First-generation progeny of immigrants had mean myoglobin levels on the order of 92.8 ng/ml. Elevated myoglobin levels were also noted in athletes and were further raised by physical training. Similarly, above-normal concentrations also prevailed in alcoholics and patient with renal disease and were corrected by appropriate therapy. Mild respiratory insufficiency was accompanied by insignificant depression of serum myoglobin, whereas more advanced stages presented with elevations. These observations suggest that serum myoglobin may be useful as an indicator of adaptive physiological changes and pathology. References 15: 7 Russian, 8 Western.

### 2D-<sup>1</sup>H-NMR Conformational Studies on Transmembrane C, F and G Segments of Bacteriorhodopsin

937C0195A Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript  
received 20 Jun 92) pp 5-20

[Article by I. V. Maslennikov, A. S. Arsenyev, L. D. Chikin, A. T. Kozhich and V. T. Ivanov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.322.5: 543.422.25]

[Abstract] 2D-<sup>1</sup>H-NMR spectra were used for a conformational analysis of synthetic analogs of membrane-spanning C (amino acid residues 67-106), E (128-162), and G (190-233) peptide fragments of *Halobacterium halobium* bacteriorhodopsin. For retention of a hydrophobic environment the peptides were solubilized in a 1:1 methanol:chloroform mixture with 0.1 M LiClO<sub>4</sub>. Combination of DQF-COSY, TOCSY and NOESY techniques and identification of interproton Overhauser effects revealed right-handed  $\alpha$ -helices in the central portions of the peptides. In the C peptide the helix involved residues Pro-77 to Val-101, and in the G peptide the Ile-198 to Arg-227 segment. In the case of the E peptide the helix encompassed virtually the entire length of the molecule from the CO group of Val-130 to the NH group of Tyr-159. Figures 3; references 35: 6 Russian, 29 Western.

### Cloning and Expression of PCR-Prepared *Staphylococcus aureus* Enterotoxin B Gene in *Escherichia coli*

937C0195D Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript  
received 14 May 92) pp 75-80

[Article by K. B. Ignatov, L. G. Chistyakova, O. B. Shemchukova, S. B. Gorodetskaya and V. I. Kiselev, All-Russian Scientific Center of Molecular Diagnostics and Therapy, Moscow; UDC 577.214.622]

[Abstract] The PCR technique was used to identify clinical isolates of *Staphylococcus aureus* bearing the SEB (staphylococcal enterotoxin B) gene (entB) and for its isolation in a 1135 kbp DNA segment bearing all the entB regulatory elements. Conventional methodology was utilized for cloning entB in plasmid pUC19, which was then used for transformation of *E. coli* JM 109. Expression of entB in *E. coli* resulted in the synthesis of an insoluble form of SEB with a leader peptide (31.4 kD) and a mature soluble form (28.5 kD). Dot-ELISA methodology showed that the yield of the recombinant toxin represented 1.7 percent of total *E. coli* protein. Figures 4; references 16: 3 Russian, 13 Western.

### Synthesis of Oligothymidilate Derivatized With Alkylating Agent and Biotin for Site-Specific Chromatin Modification

937C0195E Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript  
received 08 Apr 92) pp 81-85

[Article by A. V. Gorozhankin, Ye. M. Ivanova and N. D. Kobets, Novosibirsk Institute of Bioorganic Chemistry, Siberian Branch, Russian Academy of Sciences; UDC 547.963.32.057+577.164.187]

[Abstract] Cursory description is provided of the synthesis of an oligodeoxythymidilate derivative ((pT)<sub>16</sub>) bearing an alkylating agent (4-[N-methyl-N-(2-chloroethyl)amino]benzylamine) on the 5'-end and biotin at the 3'-end. Trials with HeLa cells demonstrated that the derivatized (pT)<sub>16</sub> molecule specifically alkylates unwound poly(dA) DNA segments. Consequently, this molecule can be used for site-directed DNA modification within the chromatin complex. In addition, such sites can be visualized by electron microscopy by complexing the biotin moiety with streptavidin-colloid gold. Figures 2; references 14: 7 Russian, 7 Western.

### Diastereoisomers of Anionic Oligonucleotide Analogs. Part 7. Synthesis and Physicochemical Properties of Diastereoisomeric Deoxydinucleoside Methylphosphonates

937C0195F Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript  
received 22 Nov 91; in final form 16 Jun 92) pp 86-94

[Article by Ye. V. Vyazovkina, N. I. Komarova and A. V. Lebedeva, Novosibirsk Institute of Bioorganic Chemistry, Siberian Branch, Russian Academy of Sciences; UDC 577.113.(4+7)]

[Abstract] A modification of the Miller method [BIO-CHEMISTRY, 25(18):5092, 1986] was employed in the synthesis of 16 pairs of diastereoisomeric deoxydinucleoside methylphosphonates in yields of 60-83 percent. Conventional chromatographic separation and reverse-phase chromatography on silicagel (Silasorb 600) yielded the same order of elution patterns for each pair of diastereoisomers. UV hypochromicity and the Cotton effect on CD spectra were greater for the diastereoisomers eluting first in each pair. Accordingly, the diastereoisomers in a given elution peak—first or second—exhibit identical configuration around the P-atom. References 21: 2 Russian, 19 Western.

### Acylovir Congeners. Part 8. Synthesis and Antiviral Activity of (R/S)-5-Hydroxy-4-Hydroxymethyl-3-Oxapent-3-yl Derivatives of Nucleic Bases

937C0195G Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript  
received 15 May 92) pp 95-102

[Article by I. P. Smirnov, T. L. Tsilevich, S. V. Kochetkova, G. V. Vladyko\*, L. V. Korobchenko\*, Ye. I.

Boreko\*, B. P. Gottikh and V. L. Florentyev, Institute of Molecular Biology imeni V. A. Engelgardt, Russian Academy of Sciences, Moscow; \*Scientific Research Institute of Epidemiology and Microbiology, Belarus Ministry of Health, Minsk; UDC 547.963.3.057]

[Abstract] The alkylating agents 1,3-diacetoxy-2-(1-acetoxyethoxy)propane and 1,3-dichloro-2-(1-chloroethoxy)propane were employed for synthesis of 5-hydroxy-4-hydroxymethyl-3-oxapent-2-yl derivatives of uracil, thymine, cytosine, adenine and guanine in an attempt to expand the scope of available antivirals. In addition, a 1,2,4-triazole-3-carboxamide analog of ribavirin was also synthesized and tested. Trials with cultures of chick embryo fibroblast cultures showed these agents to be relatively nontoxic (400-800 µg/ml), with 9-(5-hydroxy-4-hydroxymethyl-3-oxapent-2-yl)guanine identified as being particularly promising against herpes type I virus with a therapeutic index of 32. References 22: 6 Russian, 16 Western.

#### Dioxolane-Derivatized 3-Deoxythymidine

937C0195H Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript received 21 May 92) pp 103-112

[Article by Ye. V. Yefimtsova, S. N. Mikhaylov, S. V. Meshkov\*, A. V. Bochkarev and G. V. Gurskaya, Institute of Molecular Biology imeni V. A. Engelgardt and of Chemical Physics imeni N. N. Semenov, Russian Academy of Sciences, Moscow; UDC 547.854.4'455.6'118.057]

[Abstract] Search for novel agents against retroviruses led to the synthesis of new nucleoside analogs derivatized with cis- and trans-2-methyl-4-hydroxymethyl-1,3-dioxolanes. The key steps consisted of the alkylation of the sodium salt of thymine with 2-bromomethyl-4-benzoyloxymethyl-1,3-dioxolane and chromatographic separation of the cis- and trans-isomers. Debenzoylation yielded the target 3'-deoxythymidine congeners. The corresponding mono- and triphosphates were prepared in an analogous manner. Structural confirmation of the products was obtained by NMR and X-ray spectroscopies. Figures 3; references 21: 2 Russian, 19 Western.

#### Solid-Phase Synthesis of Tritium-Labeled Cytokinins

937C0195I Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript received 22 Jun 92) pp 113-116

[Article by O. V. Lushkina, G. V. Sidorov and N. F. Myasoyedov, Institute of Molecular Genetics, Russian Academy of Sciences, Moscow; UDC 547.857.7'11\*3.057:542.973.2]

[Abstract] Conditions affecting the yield and radioactivity of tritium-labeled kinetin (KIN) and 6-benzylaminopurine (BAP) in solid-phase synthesis were

analyzed for purposes of process optimization. An important finding was that presence of Al<sub>2</sub>O<sub>3</sub> in the Pd catalyst significantly reduced the yield. Maximum yields of KIN (30.0 percent) and BAP (43.0 percent) were obtained on Pd/BaSO<sub>4</sub> and Pd/CaCO<sub>3</sub> catalysts, respectively. Radioactivities of the products were on the order of 150-155 Ci/mM and represented degrees of substitution approaching 95 percent. Figures 3; references 4: 2 Russian, 2 Western.

#### Synthesis and Antigenicity of Core- and NS3-Peptides of Hepatitis C Virus

937C0195J Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript received 14 Jul 92) pp 126-129

[Article by Yu. A. Semiletov, T. V. Firsova, V. A. Shibnev and S. O. Vyazov, Institute of Virology imeni D. I. Ivanovskiy, Russian Academy of Medical Sciences, Moscow; UDC 578.891.083.3:577.112.6]

[Abstract] Solid-phase techniques were used to synthesize sequences 20-34 and 22-34 of the core protein and sequence 1269-1282 of NS3 protein of hepatitis C virus (HCV), employing Boc-Bzl strategy and activated esters. ELISA studies showed that the 20-34 core sequence reacted with 100 percent of the sera derived from patients with chronic HCV infection. Core sequence 22-34 reacted with 72.0 percent of the sera, and NS3 sequence 1269-1282 was positive in 33.3 percent of the cases. These findings suggest that the immunodominant antigenic component of HCV is located in the 20-34 segment of the core protein. References 7: 1 Russian, 6 Western.

#### Nucleotide Sequence of Phospholipase C and Sphingomyelinase Genes of *Bacillus cereus* VKM-B164

937C0195K Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript received 06 Aug 92) pp 133-138

[Article by I. V. Gavrilenko, G. Ye. Bayda, A. V. Karpov and N. P. Kuzmin, Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences, Pushchino, Moscow Oblast; UDC 577.113.5:577.212.2'152.31\*412]

[Abstract] Conventional techniques of genetic engineering were employed for the cloning and recloning phospholipase C and sphingomyelinase genes of *Bacillus cereus* VKM-B164 for transformation of *E. coli* and sequence determinations. Physical maps of both genes were obtained once they were cloned in plasmid pUC19 (EMBL accession No X64141) and compared with *B. cereus* strains SE-1, IAM-1208 and GP-4. Both gene sequences were identical to those in strain SE-1, but differed from the sequences established for *B. cereus* strains IAM-1208 and GP-4. Figures 2; references 11: 2 Russian, 9 Western.

**Novel Reagent for Phosphamidite Synthesis of Biotin-Labeled Oligonucleotides**

937C0195L Moscow BIOORGANICHESKAYA

*KHIMIYA in Russian Vol 19 No 1, Jan 93 (manuscript received 24 Sep 92) pp 139-141*

[Article by V. A. Korshun, Ye. V. Nozhevnikova and Yu. A. Berlin, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.113.6]

[Abstract] A novel phosphitylating agent—O<sup>1</sup>-(4,4'-dimethoxytrityl)-O<sup>5</sup>-(N,N-diisopropylamino-2-cyanoethoxyphosphinyl)-3-(N-biotinyl-6-aminocaproyl)-3-aza-1,5-pentanediol—has been synthesized for terminal (3'- or 5'-end) labeling of oligonucleotides with biotin. The reagent is soluble in acetonitrile and suitable for use in automatic synthesizers, with the aminocaproyl spacer providing steric freedom for complexation of the biotin moiety with avidin/streptavidin. Figures 1; references 12; Western.

## Production of Restriction Enzymes at Lithuania Enterprise

937C0190A Rotterdam NRC HANDELSBLAD  
in Dutch 23 Dec 92 Science Supplement pp 1-2

[Article by Steven Dickman: "Made in Lithuania. Lithuanian Biotechnologist Succeeds With Restriction Enzymes"]

[Text] The former Soviet Union is still completely virgin territory for biotechnology. True, the Soviet leaders did pump billions of rubles into state-controlled biotechnology industries and more scientists were trained to manage those enterprises than in any other country, but the arrival of the free-market economy signals the shut-down of practically all of those industries.

Bearing this in mind, a glimpse into the New England Biolabs 1992 catalog, a bible for molecular biologists, furnishes a startling discovery. Page 47 contains a list of a new series of restriction enzymes, the molecular "shears" that snip DNA molecules into pieces and that constitute an essential item in any molecular biologist's tool kit. The startling thing is that the enzymes bear the label *Made in Lithuania*.

Lithuania? How is it possible for a tiny Baltic country that has been independent for barely a year to duke it out with large biotechnology firms in the West to supply enzymes? Put this question to Rich Roberts, New England Biolabs research director and he will answer with a single word: "Janulaitis."

Vidas Janulaitis is professor of biochemistry at Vilnius university, head of the "Fermentas" Biotechnology Institute and, furthermore, the architect of the largest assembly of restriction enzymes in the world, offering more than a hundred of them.

Janulaitis is apparently the first successful entrepreneur to emerge from the former Soviet Union in this biotechnology sector. Even a spokesman from a competitor of New England Biolabs, Jeremy Walker, of Amersham International in Illinois, applies the epithet of "outstanding" to Janulaitis' contributions to the number of new restriction enzymes that are put on the market each year.

How was it possible for Janulaitis to steer clear of the chaos during the dismantling of the Soviet Union and put together one of the world's largest assortments of restriction enzymes? Janulaitis, whose build resembles that of a wrestler more than a biochemist, says there is no simple answer to that question. Both its appearance and the surroundings of his institute that was transformed into a company, situated on the outskirts of Vilnius, make it hard to believe that it plays a major role in the world of restriction enzymes.

The road leading out of Vilnius runs past clusters of old wooden farmhouses with sloping roofs. Mule-drawn hay-wagons creak their way forward along dusty roads. Across the road from the institute peasants manually cultivate potato fields. While lighting up the first of a

chain of strong Russian cigarettes, Janulaitis leans back and starts in on a litany of the problems that life in the Soviet bureaucracy entails. According to him, contrary to what most westerners think, the Soviet Union invested huge sums in biotechnology, and even in his own solid red brick institute. In 1975 the Microbiological Industry Ministry (in Moscow) built and staffed four enormous institutes: two in or near Moscow, one in Novosibirsk and one in Vilnius. They all received enormous amounts of money and large numbers of researchers to produce enzymes. One of the smallest, the institute in Vilnius, was given a 730 person staff.

The problem was that the managers of the institute had no concept of how the products had to be manufactured. According to Janulaitis the government poured "dozens and dozens of people and billions and billions of rubles" into biotechnology and at best this resulted in "some reasonably good basic research" but, for all intents and purposes, not in an industry that was worth all the effort.

He is quick to add that the researchers themselves were not to blame. According to him, even if they had wanted to produce what was really needed, it would have been virtually impossible for them to persuade industry to manufacture the new products. The Communist system simply provided no incentives for innovation.

## Bulk Commodities

The institute in Vilnius could easily have nourished the illusion of security because of the automatic cash flow from Moscow. But Janulaitis did not go along with that. He acknowledges that he was convinced that "the cash flow would eventually dry up. It was perfectly obvious to me that there was not a single country that could allow itself to maintain so many large institutes yielding not a single useful result."

It was Janulaitis' opinion that the order from Moscow to manufacture enzymes as bulk commodities for industry would provide little for Lithuania itself. The work was simple and could be performed elsewhere. "Besides, I realized that most of the industry in this country would not be able to operate once the country became free. It depended on Russia for machinery and raw materials. The only thing we have is our brain."

And so Janulaitis, who gradually rose in the institute to become director in 1989, veered away from bulk manufacture of enzymes for industrial use to the field in which his own personal interest lay: restriction enzymes. At the time Janulaitis reckoned that production of new restriction enzymes would require a lot of ingenuity and exertion, but it called for less costly equipment. And once the enzymes could be manufactured, they could be sold and shipped in small quantities: precisely what a small country that wanted to be independent of Moscow needed.



### Shrewd

Janulaitis was not only so shrewd as to tap into a productive research sector, but he already had a feel for the way capitalism worked. Janulaitis came from a family of Lithuanian farmers who never had anything but poor soil to cultivate. From the outset he realized that in the restriction enzymes sector, the "capital" would consist of the strains of bacteria from which the enzymes were isolated. He drove his people hard to keep searching for new varieties since new enzymes could be continuously reproduced "considering that anyone with enough perseverance and persistence can replicate your work."

Institute researchers vacationing in remote corners of the Soviet Union, sometimes as far afield as Kamchatka and Siberia, were asked to collect soil samples near springs of hot water, on high hills and in other special environments, in the hope of finding special strains of bacteria producing unique enzymes. Janulaitis even asked friends at other research institutes and hospitals to forward samples that they had assembled from the entire Soviet Union. And extensive searches were kept up close to home. These proved to be worth the effort when his colleagues discovered two unique strains of bacteria in a garden nearby the institute.

Janulaitis still clearly remembers being able to sell his first restriction enzymes as early as 1976 to Soviet laboratories. At that time he also had his first run-in with the Soviet bureaucracy. Merely one transaction with one institute "required a pile of paper this high," says Janulaitis, holding his hands a half meter apart. But Janulaitis came up with a solution that still causes him to smile: he simply gave the enzymes away.

"That did not require any paperwork," he says with a laugh. "In this way we made friends throughout the Soviet Union. In a few months everyone knew my name." And now that his institute began to be known, it earned some profit. Friends helped him pressure Moscow and four years later (called "rapid progress" at that time) he was able to obtain enough hard currency to purchase fermentation equipment in Germany.

By 1983 Janulaitis had advanced to the point of asking Moscow to approve of allowing contacts to be made with companies in the West. He wanted to try to sell them restriction enzymes as a bulk commodity that they could then resell under their own brand name. "My colleagues said I was crazy," asserts Janulaitis. "Why should you do all that extra work, they said, when all the money is just going to go to Moscow?"

But he persisted, only all too quickly to observe that his friends were right. He received orders from a Japanese company, but "when we went to sell, we did not bring in a single cent." So why did he continue on? "I just considered it a hobby of mine," says Janulaitis. But there was still another reason: "I wanted to gain experience in trading abroad."

The experience apparently paid off some years later when the era of *perestroika* dawned. By 1987 Janulaitis was in a position to have the production department of his institute registered as a semi-autonomous enterprise. And in 1988 the *Politburo* in Moscow granted the new enterprise approval to ship directly to western customers and to keep the profits. Then the Soviet Union began to disintegrate and during that process Lithuania was officially declared independent on 6 September 1991.

### Russian Transfer of Payments

However much those developments were welcomed, they did not immediately make it easier for the fledgling enterprise. The contacts that he had built up during his "hobby" with the West, plus the new possibility for unrestricted travel, resulted in orders for a series of enzymes that by that time was longer and more diversified than any others in the world. Janulaitis, however, was still wrestling with the Russian transfer of payments.

"We had to use the single bank in the entire country that was allowed to participate in foreign transfer of payments," says Janulaitis. "But the bank routinely had no cash. Although we did have cash in our account, we had to go to Moscow to have payments made. But there was no getting into the main branch of the bank in Moscow. The entrance was constantly blocked by people trying to get their money. It got so bad that the doors were finally kept shut all the time."

Janulaitis tried to remove this last obstacle in the traditional way but found himself caught up in a situation that one would expect to find in a Russian fairy tale. "Our man had to go find the back door of the bank and bribe someone to let him in. Then he located the party responsible for our transaction. They sat in a large room whose walls were trimmed up to the ceiling with dozens of receipts. The individual offered to help us, but only if we could find our receipt among the dozens of them."

Naturally this signaled the end of the fairy tale. Janulaitis' people were unable to find their receipt and had to return emptyhanded. "You may find this story amusing, but it was not amusing for us," says Janulaitis.

### Warning

Since then the situation has improved. Once Lithuania became independent the country established its own bank and this now settles transactions for the enterprise within a few hours or days. And after numerous trips to the West, Janulaitis now sells his enzymes via 15 companies in 12 different countries. His research teams (totaling 100 individuals) continue to prepare new enzymes and, according to him, do so at a faster pace than their competitors. Janulaitis will step down this year as director and his colleague, biochemist Viktoras Butkus, will take charge. According to Butkus the enterprise earned close to \$340,000 in 1991 from foreign sales.

Janulaitis hopes that in the future he will be able to put other companies in the West in contact with the former Soviet Union. "Lithuania could function as a bridge; it is a part of Europe that is familiar with the Soviet system." But he aims a stern warning at many of his former Soviet colleagues who are trying to do business with the West. "People here think that 'good business' means that it is good just for themselves," says Janulaitis.

Enterprises in the former Soviet Union often do not honor their contracts with the West and the injured party then often has no possibility of obtaining redress. Copyright and patent protection is urgently desired, but he cautions that "it will take at least a decade before businesses in the former Soviet Union will honor the many international patent agreements that were signed by Soviet officials in the final days of the Union." The biggest problem that Fermentas is now struggling with is the sorry image of the former Soviet Union. "No one

trusts us," says Janulaitis. Potential resellers of Fermentas enzymes frequently ask if they may remove the *Made in Lithuania*. "We realize that most products from the former Soviet Union are worse than bad," states Janulaitis. But he emphasizes that "our quality control is better than that of companies in the West." Janulaitis says that despite everything he states that the *Made in Lithuania* will stay in place. He claims that in this way he will have helped people mentally associate resourcefulness and top quality with Lithuania.

The startup period for capitalism in a free Lithuania is still replete with problems for Janulaitis and his colleagues. But he says there is one significant difference from before. "The only ones we can hold responsible are ourselves, whether we now fail or succeed."

*Translation by George Beekman*

**Soil Moisture and Radionuclide Mobility in Chernobyl Area**

937C0196A Moscow *EKOLOGIYA* in Russian No 2, Mar-Apr 92 (manuscript received 07 Feb 91) pp 76-79

[Article by L. N. Mikhaylovskaya, Ye. N. Karavayeva and I. V. Molchanova, Institute of Plant and Animal Ecology, Ural Branch, Russian Academy of Sciences; UDC 574:577.39]

[Abstract] Soil mobilities of Sr-90 and Cs-134 through -137 were assessed in relation to soil moisture in the 3 km Chernobyl zone. The respective baseline counts for Sr-90 and Cs-134 through -137 in the 0-2 cm soil samples were 120-130 and 200-600 kBq/kg of dry wt. Analysis of free (filtrate) and bound (adsorbed + capillary) radioactivities revealed that for Sr-90 the filtrate:bound ratio was 2.5 regardless of moisture. The corresponding ratio for Cs-134 through -137 was 1, increasing to 20 in complete inundation (300 percent over saturation). Accordingly, these findings indicate that under normal conditions soil moisture has no bearing on Sr-90 and Cs-134 through -137 migration patterns in the soil. References 7: 6 Russian, 1 Western.

**Rapid Biotesting for Assessment of Anthropogenic Environmental Factors**

937C0196B Moscow *EKOLOGIYA* in Russian No 2, Mar-Apr 92 (manuscript received 13 Nov 91) pp 94-95

[Article by A. V. Pozharov and S. A. Shelemotov, "Kvant" Youth Creativity Center for Science and Technology, St. Petersburg; UDC 574.64.084.1:593.1]

[Abstract] Determinations of threshold limit values for various toxicants in the environment has been shown to be of limited value in ecotoxicology and, accordingly, has been supplemented by biosensor methodology. The latter rely—by and large—on changes in photosynthetic reactions, behavioral parameters, and bio- and chemiluminescence. Recent developments have included the design and production of Biotestor-2 (Kvant, St. Petersburg) for monitoring tactic responsiveness of infusoria. The latter system makes possible rapid assessment of environmental changes via their impact on the behavior of a complex organism and expands the scope and reliability of environmental monitoring. References 4: Russian.

**Intravascular Laser Irradiation of Blood in Generalized Purulent Peritonitis: Impact on Erythrocyte Ultrastructure**

937C0199 Moscow *KHIRURGIYA* in Russian No 9-10, Sep-Oct 92 (manuscript received 11 Oct 91) pp 35-39

[Article by I. N. Zimon, A. I. Agzamov, V. A. Khoroshayev, Yu. I. Kalish and I. Z. Dalimov, Scientific Surgical Center, Tashkent; UDC 616.381-002.3-089+615.849.19.03]

[Abstract] Impact of intravascular laser irradiation of blood on erythrocyte status was assessed in 60 patients with generalized purulent peritonitis. The scanning electron micrographs of the erythrocytes were compared with the outcome in 60 control patients managed solely by conventional means sans laser therapy (2-10 mW/cm<sup>2</sup> laser output at 623.8 nm wavelength; 40-60 min/day for 5-10 days). Laser therapy was seen to provide objective and subjective clinical benefit, with the objective criteria evident in hematologic monitoring. In the case of the erythrocytic cell line, elevations in total erythrocyte counts and in the percentage of normal-appearing cells were attributed to laser stimulation of bone marrow and release of erythrocytes from sequestering organs. References 6: Russian.

**Collection of Capillary Blood Specimens by Laser Skin Puncture**

937C0202 Moscow *KLINICHESKAYA LABORATORNAYA DIAGNOSTIKA* in Russian No 9-10, Sep-Oct 92 (manuscript received 15 Aug 91) pp 64-66

[Article by A. M. Prokhorov, Yu. K. Danilevko, A. V. Sidorin, A. M. Nasedkin, N. Ye. Gortbatova, L. M. Roshal, V. V. Osiko and V. N. Titov, Institute of General Physics, Russian Academy of Sciences; "Astr" Center, Ministry of Health, Russian Federation; All-Union Cardiological Scientific Center and Scientific Research Institute of Pediatrics, Russian Academy of Medical Sciences, Moscow; UDC 616.15-074]

[Abstract] Trials were conducted with an erbium laser (2.94  $\mu$ m) apparatus designed for skin perforation for collection of diagnostic blood specimens. The laser created a puncture suitable for collection of 1000  $\mu$ L of unhemolyzed capillary blood that was 1.5-2.5 mm deep, 2.5 mm long, and 0.1-0.2 mm wide. Suitable energy ranges for children under three were 0.5 J, for 3- to 15-year-olds 0.7 J, and for adults 1 J. Figures 1; references 6: Western.

**Newly Identified Fungal Disease Zaaminellosis**

937C0192A Moscow MEDITSINSKAYA GAZETA  
in Russian 20 Nov 92 pp 8-9

[Article by Prof N. Dekhkan-Khodzhayeva, director, Scientific Research Center of Mycology and Protozoan Diseases, Uzbekistan Republic Ministry of Health: "Outline for the Practical Physician: Mycology. Zaaminellosis"]

[Text] Zaaminellosis is a profound mycosis proceeding predominantly with affliction of the hemopoietic and reticuloendothelial system, internal organs, especially the lungs, liver, spleen, adrenal glands, heart and kidneys, urogenital organs, the central nervous system, mucous membranes, skin, hair cover, bones and joints.

The mycosis was discovered for the first time in 1974 in Uzbekistan's Zaaminskiy Rayon, Dzhizak Oblast by N. Dekhkan-Khodzhayeva, who isolated the infectious agent from peripheral blood of patients and from soil in this territory. In parallel with isolation of cultures in blood smears from patients subjected to Giemsa-Romanowsky staining, pinkish crimson crenulated structures up to 15 microns in size were detected. Experiments showed that these are the remnants of capsules from the fungus's parasitic form. These formations came to be called serzhantellopodobnyye [sergeantella-like] formations (SLFs). See photograph.

**Etiology**

The agent of zaaminellosis is a new variant of the fungus *Paecilomyces variotii* Bainier, 1907, var. *Zaaminella* Dechkan, 1974. The isolated culture was identified at the mycology department of Moscow State University imeni M. V. Lomonosov, in the mycology laboratory of the Microbiology Institute of the Russian Academy of Sciences, and in the city of Atlanta in the United States.

This fungus is dimorphic. The mycelian form is typical of strains circulating in the environment, and when they are cultured in the appropriate nutrients. The parasitic yeast form forms in human and animal tissues. The mycelium is encrusted, and it terminates in phialides consisting of chains of oval conidia. Among other forms of sporulation, large solitary chlamydospores are encountered on side branches regardless of the nature of the nutrient medium. The chlamydospores differ sharply in their internal structure from what is published in the key (Samson, 1974) in possessing grainy contents. Inspection of the chlamydospores under an electron microscope revealed these grainy contents to be identical to conidia. They were given the name endospores on account of their location inside chlamydospores. From one to four endospores were counted inside chlamydospores depending on the stage of development.

The yeast form of *Zaaminella* is revealed in stained tissue preparations under immersion, and they are located intracellularly. In tissues, the fungal cells are round, sometimes oblong, with scalloped margins, or in



the form of blackberries from 2 to 15 microns in size depending on the stage of development. Endospores are visible within, especially with Stidman [transliteration] staining.

In the stage of active division, the yeast cells are located inside tissue cells of the lungs, liver, spleen, heart, kidneys and brain. Electromicrographic analysis of blood elements revealed intracellular duplication of parasitic forms of the fungus: Two-, three- and four-chambered formations with a clearly outlined light capsule are evident within leukocytes, monocytes, lymphocytes and erythrocytes.

Such a phenomenon, where one agent totally afflicts the entire hemopoietic system and all organs and tissues, was heretofore unknown. This is a discovery. *Zaaminella* spores are resistant in the environment, maintaining their viability over a long period of time. Formalin and carbolic acid kill the fungi in 1-4 hours at a solution concentration of 5-10 percent. Boiling kills the fungi instantaneously. The tissue or parasitic forms are less resistant to desiccation, the action of ultraviolet rays and disinfectants.

The geographic distribution of *Zaaminella* was studied by revealing SLFs in blood smears and isolating cultures of this fungus from soil of different oblasts and rayons (the work is ongoing).

The results of testing blood for SLFs and isolating cultures from patients at therapeutic, surgical and obstetric-gynecological hospitals in other Central Asian republics and Afghanistan indicate that this agent and the diseases it evokes are widespread. Failure to diagnose the disease occurs because physicians are not alerted to it and they are not knowledgeable in mycology; cases of zaaminellosis in Sillamyae, Chernovtsy and Novosibirsk are examples. In these cities, the clinical pattern of disease varied from focal alopecia to terminal severe sepsis.

**Epidemiology**

Zaaminellosis occurs at any age, but the frequency of infection of children is 10 times higher. The disease is not contagious. Infection by *Zaaminella* fungi occurs when the spores are inhaled with dusty air. Fungal spores were discovered in moist soil at different levels, from 3

to 15 cm deep. Children may be infected in utero, by breast feeding, and during transfusions of blood and plasma. Blood-sucking insects also probably have significance to the spread of this infection—mosquitos, gnats, and wood lice, from which *Zaaminella* cultures have been isolated. Dairy products that are not heat-treated (sour cream, butter, cottage cheese) play an important role in the spread of zaaminellosis, since SLFs were detected in 35.2 percent of cattle.

Thus the principal pathways of infection of adults by *Zaaminella* are: aerogenic, with food, and during blood and plasma transfusions. Children are infected primarily in utero and by breast feeding.

In adults, fungal spores that enter the respiratory tract settle in bronchioles and alveoli and transform into the parasitic yeast-like form. From here, the fungi spread with the bloodstream to different organs and tissues. *Zaaminella* is predominantly a blood parasite, evoking generalized, rapidly proceeding septic forms of disease. Death is often observed due to failure of prompt diagnosis, especially in children in the pre- and postnatal period. Zaaminellosis is the principal cause of growth of child mortality.

Patients are dominated by persons with sluggishly proceeding forms, with frequent recurrence, and with affliction of single or several organs. The lungs are afflicted most often, in which case enlargement of mandibular lymph nodes is noted. The disease proceeds in mild form. Sometimes infected individuals remain practically healthy.

In other cases entry of the disease agent into lung tissue may be accompanied by profound localized affliction of the lungs taking the form of infiltrates, predominantly in the right lung.

In young children, dissemination of the fungus proceeds unhindered in the body due to the absence of immunity. The agent penetrates through the gastrointestinal tract and lungs into the bloodstream and into lymph nodes. The process becomes generalized. In these cases pathohistological analysis reveals fungi in all organs and tissues, being the cause of death.

Pathomorphological analysis of organs of 145 children from one month to three years old that died in resuscitation wards revealed parasitic forms of the fungus in the lungs, heart, liver, kidneys and brain of 84 (57.8 percent) of the children. Because of the process's generalization, the disease proceeds with various clinical manifestations, masked by diseases of the ear, nose and throat and by frequently recurring pneumonia, which transform into obstructive bronchitis and bronchial asthma due to the body's sensitization.

It should be noted that parallel affliction of other organs manifests itself clinically by an increase in the dimensions of the liver (hepatitis), pyelonephritis, skin afflictions in the form of neurodermatitis and psoriasis, and focal hair loss. Locating themselves in blood vessels of

the lower limbs, the fungi afflict the vascular intima, evoking thrombophlebitis, endarteritis and vasculitis. Fungi were discovered histologically in thrombi removed from 66 percent of patients with vascular pathology of the lower limbs.

We observed affliction not only of vessels but also of brain tissues, in which case the disease proceeded clinically as meningoencephalitis.

In renal tissues, fungi multiply in glomeruli and in the ascending and descending loops, establishing themselves intracellularly. Clinical disease takes the form of persistent pyelocystitis, pyelonephritis and polycystosis, transforming into chronic renal insufficiency.

Affliction of genital organs occupies a special place, manifesting itself as endometritis, adnexitis, cystic affliction of the ovaries, infertility, recurring miscarriages, and the birth of dead or weakened children. Our examinations of infected mothers also revealed chronic vulvitis and vulvovaginitis.

Infection of genital organs through blood evokes a broad spectrum of diseases, and when conception occurs, the process spreads to the fetus, which leads to various pathology and abnormalities, thus influencing the population's reproductive potential.

When the fungus enters the human body, antibodies form—agglutinins and precipitins.

Antigen prepared from the mycelian forms of the fungus produced results in the hemagglutination reaction permitting the hope that serodiagnostics could be developed for zaaminellosis. Efforts to isolate species-specific antigen and a diagnosticum are continuing. Colonization of monocytes, lymphocytes and neutrophils is a delaying factor of both cellular and humoral immunity, leading to development of immunodeficiency in two-thirds of the patients, while affliction of erythrocytes by these fungi and their reproduction evokes anemia.

Specific allergy is distinctly expressed in the presence of zaaminellosis, manifesting itself as neurodermitis, dermal pustulous diseases, psoriasis, vitiligo and aleukia, as well as focal and total hair loss, including eyebrows and eyelashes.

Weakening of hair cover and appearance of small and large balding spots are noted 1-1.5 months after experimental infection of animals (rats, mice).

### Clinical Pattern

The clinical pattern of zaaminellosis is characterized by polymorphism: From pulmonary acute respiratory diseases and asymptomatic forms, to severe, often generalized afflictions with a lethal outcome. The results of clinical study of over 5,000 patients—children and adults—served as the grounds for developing a classification of this infection.

## CLASSIFICATION

### 1. Pulmonary zaaminellosis:

- a) acute respiratory disease;
- b) pulmonary zaaminellosis (light, moderately, severe course);
- c) chronic zaaminellosis.
  - 1) frequently recurring form of pneumonia
  - 2) interstitial pneumonia
  - 3) mediastinal form
  - 4) tracheobronchitis, laryngitis, bronchitis with obstructive syndrome
  - 5) bronchial asthma.

### II. Acute disseminated zaaminellosis.

### III. Chronic disseminated zaaminellosis with affliction of lungs, liver, heart, kidneys, blood, hemopoietic organs and the urogenital system.

### IV. Chronic zaaminellosis of the skin and hair cover.

The asymptomatic form of pulmonary zaaminellosis with positive SLFs was observed in patients with several petrifications, usually at the hilum pulmonis. Acute pulmonary zaaminellosis begins with disease of the ear, nose and throat, and on the second or third day total bilateral pneumonia develops in the lungs with moist rales of different calibers.

The course of disease is atypical, there is no labored breathing or cyanosis of the nasolabial triangle, and the overall state remains satisfactory even in the presence of high temperature. Enlargement of mandibular, posterior cervical, axillary and inguinal lymph nodes is noted. High temperature persists up to one week, after which it lowers to a subfebrile state; it was observed to increase in the afternoon.

As for the blood, slight neutrophilic leukocytosis, lymphocytosis, and a tendency toward anemia are observed, and the erythrocyte sedimentation rate of two-thirds of the patients is elevated.

**Radiological data.** Foci are noted: shadows appearing as wads of cotton, an intensified bronchovascular pattern and enlargement of the shadow of the lung roots. We observed this radiological pattern in 65 percent of patients with acute pulmonary zaaminellosis. Physical signs of 35 percent of the patients did not correspond with radiological data.

Patients were dominated by persons with a chronic, frequently recurring course of disease. It usually began acutely, with a high temperature, as otorhinolaryngological disease. Physical signs appear after 2-4 days (moist rales of varying caliber). In these cases radiology reveals

bilateral pneumonia, enlargement of all groups of lymph glands, and enlargement of the liver and spleen.

Enlargement of the liver is noted in the presence of chronic zaaminellosis in 70 percent of patients, while enlargement of the spleen is noted in 40 percent. Their dimensions and density depend on the number of times the disease recurs.

Study of the outpatient charts and disease histories of zaaminellosis patients showed that children up to 3 years old suffer the disease from 5 to 15 times, and in its severe course at that, requiring hospital care. In some of the children the process begins in the bronchi, and it proceeds clinically as bronchitis with the obstructive syndrome. A typical feature of obstructive bronchitis accompanying zaaminellosis is attacks of dyspnea at night, toward morning, while labored breathing is not noted during the day. Such a pattern was observed in 45 percent of the pulmonary zaaminellosis patients. In 8 percent of the patients the disease proceeds with phenomena of bronchial asthma that are aggravated in the spring and fall; we hardly ever observed "status asthmaticus."

Second in frequency of affliction is pathology of the skin and hair cover. Skin diseases proceed clinically in children and adults in the form of diffuse neurodermatitis, pseudofurunculosis, and large pustules that leave behind pigmented areas after healing. Diffuse or minor focal psoriasis and pseudopsoriasis and vitiligo were also observed.

Affliction of hair cover manifests itself as focal and total alopecia. All of the hair cover is afflicted in the presence of total alopecia.

Acute disseminated zaaminellosis usually proceeds as sepsis with a high temperature of up to 41°, headaches, hemorrhagic eruptions on the palms and on the soles of the feet, enlargement of the liver and spleen, leukocytosis, growing anemia, and an increase of the erythrocyte sedimentation rate. Eosinophilia is noted in some patients, as many as up to 87 percent. Such patients are usually hospitalized in infection and hematological hospitals, from which they are transferred to the republic center after infectious diseases are excluded.

In children, sepsis proceeds on the background of pneumonia, meningoencephalitis and pustulous diseases of the integument. It should be noted that we have described the most frequently encountered symptoms. A separate article could be devoted to each nosological form.

### Diagnosis

Analysis of blood smears subjected to Giemsa-Romanowsky and Heidenhain staining reveals SLFs.

Cultures of fungi from peripheral blood, breast milk, umbilical blood and sputum were isolated after these materials were seeded in the following media: Saburo, oat, potato-carrot, potato-glucose, liver and others. The morphological description of the isolates did not change with growth in different media.

Serological methods are presently being developed for diagnosis of mycosis by means of the passive hemagglutination reaction and ELISA. The immune status of zaaminellosis patients is being determined. Research aimed at creating a vaccine has been started. Peripheral blood and plasma cells are being subjected to electron microscopy with the goal of detecting *Zaaminella* in them. Bone marrow and biotates of lymph nodes are being investigated for the presence of fungi in them. Pathomorphological analysis of organs and tissues of decedents is being conducted on a large scale.

### Treatment

Upon establishment of a diagnosis of zaaminellosis, specific antifungal therapy with Amphotericin B is prescribed. The drug is prescribed in accordance with instructions, depending on the patient's weight. Amphotericin B is toxic, and it elicits a rise in temperature, headaches, chills and nausea. We administered a lytic mixture intravenously for premedication purposes. Subsequent administration of Amphotericin B produced practically no side effects, which made it possible to use the drug in outpatient conditions.

Internal treatment consisted of cycles of the locally produced drugs amfoglyukamin, mikogeptin and grizeofulvin (up to four cycles of 10 days each), and antirecidivist treatment was conducted after 3, 6 and 12 months.

Among foreign drugs, Nizoral and Diflucan produced a good effect. The drugs were used depending on age.

Besides specific therapy, we prescribed symptomatic treatment: group B and A vitamins, ascorbic acid and nicotinic acid. Special mention should be made of the positive impact of using vitamin A in injections in the presence of afflictions of skin and hair cover. When immunodeficiency was revealed, we prescribed immunomodulators—taktivin and timolin.

Positive results were enjoyed from complex therapy in 80 percent of the cases. Antirecidivist treatment provided after particular times reinforced the attained effect and prevented recurrence of disease.

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### Alopecia Caused by Fungal Infection and Giardiasis

937C0193A St. Petersburg TSITOLOGIYA in Russian  
Vol 34 No 4, Apr 92 pp 18-19

[Article by R. Yu. Alimdzhanova, N. A. Dekhkan-Khodzhayeva and M. A. Gazikhodzhayeva, Scientific Research Institute of Medical Parasitology, Uzbekistan Ministry of Health, 700107, Tashkent]

[Text] Hospital visits by patients suffering total or partial hair loss from the hairy part of the head, the eyebrows, eyelashes, and other parts of the body have grown more frequent in recent years. Between 1986 and 1990 we were visited by 68 adult patients, clinical examination of whom established a fungal disease elicited by *Paecilomyces varioti* Bain. var. *zaaminella*. This diagnosis was confirmed by the results of effective antifungal treatment of all but nine patients. Detailed examination of these patients revealed *Giardia* in them: cysts in feces and vegetative forms in duodenal contents. In addition to general fortifying and antifungal treatment, these patients underwent three cycles of anti-giardiasis treatment (anti-giardiasis drugs and therapeutic duodenal probing). Complete restoration of hair occurred in 52 patients as a result of anti-giardiasis and antifungal treatment. Thus our research and clinical observations showed the etiological role played in alopecia by the previously unknown fungus *Paecilomyces*. The combination of fungi and protozoans makes restoration of hair in patients significantly more difficult.

### Proteus-PPM Nutrient Medium for One-Step Isolation and Identification of Proteus, Providencia and Morganella

937C0200C Moscow KLINICHESKAYA  
LABORATORNAYA DIAGNOSTIKA in Russian  
No 9-10, Sep-Oct 92 (manuscript received 22 Jul 91)  
pp 59-61

[Article by Ye. P. Sivolodskiy, L. M. Gerasimenko and A. A. Koleyka, Military Medical Academy imeni S. M. Kirov; No 2 Inter-Rayon Clinical Bacteriology Laboratory, St. Petersburg; UDC 579.842.22.083.13/.18]

[Abstract] Isolation and identification of *Proteus*, *Providencia* and *Morganella* was made possible as a one-step process using the newly-formulated *Proteus*-PPM nutrient medium. The medium—35-36 g nutrient agar from fish hydrolysate, 0.8 FeCl<sub>3</sub>·6H<sub>2</sub>O, 0.2 g L-tryptophan, 0.9 ml of 40 percent sulfonol and distilled water to 1 L, pH 6.8-7.2—yielded a dark-brown color around colonies belonging to the *Proteus*-*Providencia*-*Morganella* group after 20-22 hours of incubation at 35-37°C. Subsequent fermentation studies in planchettes for one hour led to the identification of *Providencia* (mannose +), *Morganella* (urea +) and *Proteus* (mannose -). The specificity and sensitivity of *Proteus*-PPM medium for the group were 100 percent and 92.1 percent, respectively. References 10: 9 Russian, 1 Western.



### Scarce Medicines Only for Hard Currency

937C0177A Moscow MOSCOW NEWS in English  
No 45, 8-15 Nov 92 p 10

[Article by Tatyana Koshkareva and Vladimir Shkatov]

[Text] Today Moscow has 10 chemists, a few sections at municipal pharmacies and several kiosks at specialized clinics for the elite all selling medicines for hard currency.

Most of them are joint ventures. However, since becoming independent on June 1, 1992 many of Moscow's chemists have been trying to improve their financial situation by opening sections selling drugs for hard currency only.

On average, there are several dozen customers per day, but their number is growing, and not owing to foreigners, since 80 to 90 percent are Russians. It is noteworthy that sale in such drug-stores sharply goes up in the periods when planned deliveries to the municipal shops are upset. The main demand in them is for antibiotics, vitamins, antiseptics, cardiovascular preparations and medicines of the venerotrichomonological group. Such shops have a few hundred different medicines. One of them—Pharmacy—for the elitary [as published] public opened at the Eye Microsurgery Complex has 500 medicines in all pharmacological groups and the hard currency section of chemists No. 176 has about 50 of them.

The hard currency sections receive their supplies under a state programme on agreement with the semi-commercial Pharmimex association of Russia's Ministry of Public Health. But monthly requests for a fixed list of vitally important medicines, including about 270 items sold for roubles, are met not full (ten packs of each preparation in the chemists No. 176). Pharmimex exchanges currency at the rate of 29 roubles per dollar.

The prices are fixed by suppliers. On the whole, in Moscow's hard currency chemists and the sections, they are higher than the average prices in Europe. For example, in Pharmacy, considered to be one of the most expensive, they are on average 10-15 percent higher.

Pharmacological supervision at hard-currency chemists is exercised by the Pharmacy Chamber which started functioning on August 1. It believes that in the near future there will be more chemists and sections in municipal pharmacies selling medicines for hard currency. Ordinary ones are now eagerly concluding agreements for commercial supplies of medicines from abroad.

### Avitaminosis in Russian Population

937C0179A Moscow TRUD in Russian 19 Dec 92 p 4

[Article by Prof. V. Spirichev, corresponding member of the Academy of Technological Sciences: "Health Is Sold at the Pharmacy: May It Always Be Inexpensive!"]

[Excerpts] In 1535, the expedition of Jacques Cartier disembarked on the shores of Newfoundland—or more precisely, what was left of the expedition. Over the period of time they sailed the Atlantic, most of the crew died of scurvy, and the rest were seriously ill. Expecting death, the seamen erected an image of Christ on the shore and prayed to him for a miracle. A miracle did follow, but not from the sky. It was in the form of an Indian who gave them a conifer broth to drink. That, apparently, was the first time the Europeans were acquainted with the miraculous effects of one of the most important vitamins—ascorbic acid, or vitamin C.

The time has past when vitamins represented mysterious substances with a special "life force" (*vita* is Latin for *life*). We know their chemical structure and properties, we can synthesize them and produce them on an industrial scale, and we are aware of their role and of the mechanism of action in the body.

Vitamins are absolutely necessary for normal metabolism and the biochemical support of all vital functions of the body. No child, no adult, no elderly person could exist without them.

Unfortunately, Mother Nature has set things up so that our bodies are incapable of synthesizing those vitally important substances independently: our bodies must receive them in ready-made form—in food or, if the food doesn't have enough vitamins, in the form of special vitamin additives and preparations.

But what is the situation with the supply of those biologically valuable food substances to the populace of Russia?

The answer to that question is provided by massive examinations that are regularly conducted by the Vitamin and Mineral-Substances Metabolism Laboratory of the Russian Academy of Medical Sciences Institute of Nutrition in various regions of the country. The results of those examinations clearly point to an extremely poor situation: the massive spread of latent and, sometimes, clear forms of vitamin deficiency—so-called hypovitaminoses.

The biggest problem is with vitamin C, a deficiency of which is identified in 80-100 percent of the people. Some 40-80 percent don't have enough vitamins of the groups B and A.

Here are just a few examples. An examination performed in 1990 in August (the most favorable time of year in terms of supply of vitamins) identified a vitamin C deficiency in 92 percent of the workers studied at the Uralmashzavod in Yekaterinburg: the blood levels of the vitamin were two- to fourfold lower than the acceptable level. Seventy percent of the workers showed low levels of vitamin B<sub>1</sub> and folic acid. Preschool and school-age children had deficiencies of vitamin C and the B group in 60-70 percent of cases.

A vitamin C deficiency was observed in 82 percent of the workers at the machine-tool plant in Yoshkar-Ola who were examined in the winter of 1992; in 90 percent of the vo-tech students; in 87 percent of the patients in the municipal hospital; and in 64 percent of pregnant women. Eighty to 90 percent of those examined had a deficiency of vitamins of the B group.

Similar data were obtained in children, women of child-bearing age, and blue-collar and white-collar workers of various professions in Moscow, Orenburg, Kemerovo, Novokuznetsk, Krasnoyarsk, and Norilsk; in petroleum workers of Tyumen; in river workers of the Ob-Irtysh, Yenisey, and Lena basins; and in residents of the Tula and Bryansk oblasts and the regions that were affected by the Chernobyl accident.

Low vitamin levels that have acquired a massive, constant nature are an extremely adverse factor that does substantial damage to people's health.

A vitamin deficiency lowers immunity and resistance to colds and other illnesses, worsens endurance and efficiency, enhances the negative effect of harmful environmental factors and radiation, makes the course of any ailment more severe, and hinders the treatment of ailments.

A lack of ascorbic acid facilitates the development of atherosclerosis, ischemic heart disease; cholesterol deposits in the aorta are greater the worse the deficiency in that vitamin are.

A lack of carotene and vitamin A increases the risk of certain forms of cancer. It's no accident that one of the 10 precepts for the prevention of cancer developed by the School of European Oncologists says, "Consume more vegetables, fruits, and vitamins."

A lack of vitamins during childhood and the teenage years has a negative effect on physical development. Children grow up weakened, they are often sick, and the seeds of future ill health are planted in them in the early years.

But what about the consequences of vitamin deficiency during pregnancy, when a woman's needs for vitamins are especially great? A lack of vitamins can be the cause of miscarriage, premature birth, congenital deformity, and developmental problems in an infant.

With rising prices and the food crisis, if measures aren't taken, vitamin deficiency could lead to massive avitaminosis with the most severe of consequences: the press has already reported cases of scurvy in Kostroma. A month ago, we found a clear case of beriberi (B<sub>1</sub> deficiency) in a young woman who, by the way, is a physician by profession.

So what can be done? How can we avoid the vitamin famine? In answer to that, I don't want to repeat the advice that's been mouthed so much: consume more greens, vegetables, and fruits. First of all, because that's something that everybody knows. Second, because many

can't afford to follow that advice. Third, because fruits and vegetables are far from the reliable source of vitamins that many think them to be. From them, and not from them all, we can get ascorbic acid and carotene. As for the rest of the vitamins, providing our bodies with them requires other products that are, as a rule, high-calorie, expensive, and not always accessible. For example, the richest source of vitamins B<sub>1</sub> and B<sub>6</sub> [second vitamin subscript not legible in source] is liver, and those vitamins are also in meat, black bread, buckwheat, millet, and oatmeal. We get vitamin B<sub>2</sub> primarily from milk. The main source of vitamin A is butter, and that of vitamin E, vegetable oil.

And now for a few figures. To meet one's needs for vitamins B<sub>1</sub> and B<sub>6</sub>, an individual must eat nearly a kilogram of black bread a day, or a half kilo of meat. Fifty to 100 years ago, when the energy expenditures of the population were two or three times higher than now, such volumes wouldn't have surprised anybody: the diet of a Russian soldier included 1 kg 300 g of black bread and a pound of meat every day. Who these days can allow himself such quantities—and not because of the expense, but simply because of the danger of overeating. Calculations show that a diet of 2,500 kilocalories—and that's the average energy expense of modern man—consisting of the very best products meets the needs for most vitamins by no more than 80 percent. But in the actual diets of most people, those vitamin levels are considerably lower.

Isn't that one of the reasons that, with all the information we have about the benefit of vegetables, we have in this country massive hypovitaminosis?

Hence, without in any way belittling the importance of greens and fruits or the need to correct our diets with nutritional products that are rich in vitamins (e.g., black bread instead of white bread, and buckwheat and oat porridge instead of vermicelli and macaroni), we need to point out the most reliable, effective, economic, and, therefore, massive means of preventing hypovitaminosis—the regular ingestion of multivitamin preparations that are specially designed to supplement the inadequate intake of vitamins from foods, such as Revit, Askorutin, Glutamevit, and an array of others.

A unique feature of those preparations is that, unlike medicinal preparations, they contain in one lozenge or tablet the average daily allowance of vitamins corresponding to the physiological needs of the body.

Revit contains four vitamins: A, C, B<sub>1</sub> and B<sub>2</sub>. Glutamevit contains a broader range of vitamins, seven in all: A, C, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, PP, E, plus folic acid, rutin, and a complex of trace elements.

Both those preparations must be taken daily, one lozenge or tablet after eating, and not for a short period of time, but all the time, especially during the winter and the spring, when the vitamin deficiency grows.

For a faster replenishment of vitamins in people who haven't taken vitamin preparations for a long time or who haven't ever taken them and whose vitamin deficiency is especially great, those people are advised to take one lozenge (or tablet) twice a day for the first few weeks, and then they can switch to the one-a-day regimen.

It is also recommended that for the first two weeks, one multivitamin lozenge be combined with one tablet of ascorbic acid (50 mg or 100 mg), since the ascorbic acid deficiency is the greatest. Smokers and individuals who work in hazardous workplaces should make the combination of multivitamin and ascorbic acid permanent. [passage omitted]

Unfortunately, a segment of our population and even some of our medical workers have a cautious attitude about vitamins "from the pharmacy," as if they were drugs. But vitamins—in their role and design—are not drugs. They are nutritional substances that are needed by the body.

The vitamins produced by the medical industry are not some sort of synthetic substitutes: they are absolutely identical to the vitamins that exist in food in terms of chemical structure and biological activity.

They are assimilated marvelously, and in the body they perform all the functions inherent in them quite well.

Regular daily ingestion of multivitamins in quantities that meet the physiological needs of the individual can only eliminate vitamin deficiency in the diet and cannot lead to an excess (hypervitaminosis).

Not only are vitamins from the pharmacy the most effective, they also represent the most economical means of providing the body with those biologically active food substances. Even after the considerable hike in prices for vitamin preparations, the provision of all that one person needs for a year takes only 100-120 rubles, or 30 kopecks a day. To get the same quantity of vitamins from fresh food products would take, at today's high prices, upwards of tens of thousands of rubles, even in the spring and summer.

And even though they say that "you can't buy health in a pharmacy," this is a case in which you not only can, but must, buy your health.

#### **Veterinary Vitamin Products To Improve Food Quality**

937C0179B Moscow TRUD in Russian 19 Dec 92 p 4

[Article: "Ascorbic Acid for the Cows"]

[Text] We know that the individual's health is determined primarily by the cleanliness of the air that he breathes, by the quality of the water he drinks, and the nutritional value of the food he eats. At this point, the residents of almost any population center know much about the sources that pollute the air and where they live.

Water quality is always determined when any permanent water-supply source is set up. But monitoring the quality of food, especially food of animal origin, is considerably more complex. But there are reference points here. From "healthy animals" we get "healthy food products," not only in a sanitary sense, but also in an overall hygiene-related sense, to include ecological concerns, as people are given to say these days.

In recent years, the breakdown of intereconomic ties and the decline in vitamin production have had a dramatic effect on not only the health of people, but also, to a large extent, on the state of health of animals. Failing to get in their food the biologically active substances that are necessary for growth and productivity, animals (especially swine and poultry) are not growing as much as they should, are having a harder time taking stress, are becoming more sensitive to toxic residues and nitrates in their feed, and are becoming ill more often. The meat, eggs, and milk from such animals is of low quality and is sometimes even hazardous to human health. In order to obtain good, healthy products from animals, we must see to it that their feed has the full nutritional value. The feed must contain, in the proper quantities, the full complement of the vitamins they need. When the natural content of those vitamins is insufficient, pharmaceutical additives are introduced. And that is where a competition develops between man and animal for those scarce additives—preparations of vitamins A, B, C, and others. Vitamin production needs to be expanded, and ways have to be found to use high-quality waste products, preparations produced with new technologies, and byproducts with vitamin activity.

The Belgorod Vitamin Combine has mastered and perfected a technology for the production of new preparations of ascorbinates based on ascorbic acid and vitamin A—natsevit, kaltsevit, A-natsevit, and A-kaltsevit. In terms of physiological properties, they surpass ascorbic acid. Research performed by the Laboratory of Biologically Active Substances of the Belgorod Agricultural Institute has shown that those preparations improve the health of livestock and poultry, lower their sensitivity to stress, and increase body mass and egg production. Cows that have received ascorbinates show accelerated rates of the elimination of nitrates. And most important, the hygiene-related and consumer quality of meat, eggs, and milk have improved considerably. Now under way is the manufacture of beta carotene, the indispensable provitamin A whose use in animal husbandry increases fertility 1.5- to twofold.

#### **Privatization Said To Harm Pharmaceutical Industry**

937C0179C Moscow ROSSIYSKAYA GAZETA  
in Russian 22 Dec 92 p 3

[Article by Yevgeniy Panov; "A Ton of Laxatives, or Handful of Wild Strawberries?: Will the Privatized Pharmacy Help the Patient?"]

[Text] Everybody knows that the drug situation in the country is bad. In one White Paper—a government report on the state of health of the populace of the Russian Federation in 1991—we read that the average level of drug availability was about 70 percent. The prognosis: The pharmaceutical industry in 1992 can cover a third of the needs of Russians for drugs, but with a rise in prices, it can cover a half of those needs. At a seminar near Moscow, in Golitsyn, where sector workers were thinking about how they would continue to live, the shortage of drugs and their low quality were named among the chief ills of health care. If in better times the list of pharmaceuticals accessible to the public contained roughly 6,000 drugs, now that list is one-tenth that size. There aren't enough drugs for diabetics and asthmatics, when the availability of such drugs aren't simply a matter of health, but of life and death. The common analgin has become a problem. At the same time, the factory warehouses are crammed with drugs, and their sales have dropped by one-third. The pharmacies aren't taking them—they can't sell them, because they're expensive. The "markups" of industry and commerce (up to 230 percent if they are to survive) are making our drugs a luxury, and imported drugs, debauchery. Fewer imported drugs were bought this year than were bought in the past, but, perhaps for the better, thousands of pills are gathering dust in the shop windows. A tablet valued at \$1 costs 600 rubles [R] in a Russian pharmacy. It's madness.

There's clearly a method to the madness—it's a system for financing health care. Let's take a look at the White Paper. Great damage was done to drug availability by an investment policy of three decades that was geared to import purchasing. The pharmaceutical industry of the USSR drew virtually no investments and gradually collapsed (depreciation of fixed capital reached 70-80 percent). And that was 70 enterprises and 45 research institutes employing 120,000 people. A large and better part of the pharmaceutical facilities have moved to Russia. And consequently, a large part of the problems.

As overly simple as it may sound, solving those problems just takes money. How much? About \$1 billion. Then we would get a normally functioning drug market about the year 2005. So thinks the general director of the Moscow-based NPO Biotekhnologiya, R. Vasilov, who outlined for the Golitsyn seminar participants a rough model of what the pharmaceutical industry of Russia should look like. He concluded that since the chances of getting the money from the government are pretty slim, the most realistic path to take is privatization of the enterprises. It's the most realistic path, but perhaps not the best and certainly not without its problems.

It seems to me to be not so much problematic, as downright dangerous. First, for the time being privatization Russian-style would only worsen the situation for the consumer. Drugs are vitally important, and what assortment and at what prices would the owners of pharmaceutical factories—be they domestic collectives or foreign capitalists—offer the drugs to the people?

Their egos are capable of inducing a real plague. Second, the future "normal drug market" of Russia is troubling. Because in it the normal drug business operates according to its own normal laws. And that business aims not simply to manufacture a multitude of drugs that are good and varied, but also to create ever newer drugs. Its unrealized but still hidden goal, its dream is to build a world in which the workings of the stomach are regulated by a ton of laxatives, not a handful of wild strawberries.

Now the international pharmaceutical market is ready to offer the consumer 75,000 drugs (other sources say 60,000). How many of them do we actually need to live and survive? One one-hundredth. That's a minimum. And we have to guarantee that they available. How many do we need to have after that? Six thousand drugs, as in the past? Ten thousand, twenty thousand? A laxative isn't wild strawberries. Any drug is a biological weapon. And sometimes a very strong one. And if the average American consumes \$130 worth of chemicals a year, while a Russian consumes \$8 worth, if our average citizen swallows fewer pills than does a citizen of any civilized country, that's really not so bad. It's in this very area that we don't need to be like the civilized countries. After all, it's not the amount of tablets swallowed that is important—it's other indicators, like morbidity and mortality rates, active life, and life span. We don't have anything to be proud of, we live about 10 years less than other parts of the world. But it's not just because of the shortage of drugs. There are plenty of other factors shortening our lives.

I shared all those thoughts with R. Vasilov after the seminar. Do we really need to rush into privatizing the pharmaceutical industry? Are there any other paths we could take? In Russian there is a state monopoly that is typical of the rest of Eastern Europe, a monopoly that makes private investment impossible (and, as already said, we can't count on state investment). "They're absolutely impossible to take," Vasilov stressed. For example, Russian entrepreneurs who decided to get involved in the drug business did not invest money in Russian plants—they bought drugs in the West. Privatization is already in the cards for us. And that means that the drug market and the drug business are inevitable. But not on the Western model.

Just what is the pharmaceutical industry in the West? It's a standard of progress, a leader in the field of new technologies. And what is big pharmaceutical business? It's firms that have an annual commodities turnover of \$1.5 billion, as much as a fourth of which is spent on scientific research. A total of 97 new drugs have appeared in the world over the last 15 years. Forty-seven of those drugs were developed in the United States, and not a single one was developed in our country. And it's understandable why. The development of a new preparation takes 10 years and \$100-500 million. And that money is recovered. The drug business is very profitable. In terms of profits, the drug business is comparable to the electronics industry.

It's clear that Russia will never reach such a level. And thank God for that. The world is flooded with chemical regulators, stimulants, and tranquilizers. Drink a soporific, and you'll find yourself in the tenderest arms of Morpheus. Steroids can make you like Heracles. Stiff competition leads to the appearance of forms that are ever more refined, ever more potentially dangerous. On the other hand, says Vasilov, five of those 10 years that we lose to the rest of humankind are due to the drug shortage. For that reason, we need some sort of middle version, a "respectable industry" that consists of several hundred firms, that is adapted to local raw materials and conditions, that provides people with the drugs they actually need. The probability of its being competitive on the world market is virtually nil, but it obviously needn't strive to be competitive.

It's hard to argue with that if you've killed a week looking for analgin. But it's also hard to not argue. Because after the pharmaceutical industry of Russia of 2005 has absorbed a billion dollars, it will be just as behind as the industry of 1992. It will clearly be second-rate and without a future. And as long as not a single cent or kopeck is invested in it, it's worth thinking about other paths and approaches.

The West, overfed with chemicals, is slowly, but surely beginning to see the light. It's beginning to understand something elementary: a handful of wild strawberries is better than a ton of laxatives. Production is being set up for the manufacture of preparations from herbs and any agent in general that could be regarded as part of folk medicine or old, traditional medicine. In the opinion of R. Vasilov, that area has a big future. In the next few years, however, it will become a deciding factor. Traditional medicines work: as a rule, today's individual prefers a shot of an herbal concoction. The pharmaceutical business is powerful and influential. In the end, chemical-based drugs are dangerous and harmful, but effective.

That's how things are in the West. That's not quite how they are in Russia. We don't have a powerful pharmaceutical lobby here. Miracle drugs are available to the minority. The man on the street treats a cold with raspberries, he makes a brew with whortleberry leaves, he drinks St. John's wort with mint—and that's in the capitals as well as out in the burghs. Folk medicine is nothing new to us. It suits us. We can get along with it—not like an entire pharmaceutical army, of course (without antibiotics or hormones we couldn't get by), but like forward observers. And in 15 years, we could produce—along with a respectable, if second-rate, industry for the manufacture of chemical-based drugs—promising, competitive production of nonchemical-based agents.

But the choice of a direction is a strategic matter. It's a matter of national policy in health care. Pharmaceuticals is a sphere that is so socially important, and changes there are so sensitive, and any decisions are so crucial

that, throughout the world, it is overseen by the authorities and enjoys the protection of the state. The drug market is regulated everywhere, and prices are controlled by the government. Everywhere, except in the United States. (Our "free-floating pricing" is a caricature of the American arrangement.)

It would be unfair to accuse the Russian government of indifference in this sphere. At the Golitsyn seminar, the deputy minister of health, A. Vilken, promised that the ministry would maintain control of the privatization of the pharmaceutical industry for five years. The ministry would issue a report on the consequences of the Russian-style privatization. But what does it intend to do? Create a special oversight agency. One might well expect that it will start to issue orders. We're doing the same thing that people are doing, but getting the opposite effect.

It's not wise. The health of the nation cannot be the concern of an agency, it's the concern of the state. It's not the concern of the executive or legislative authorities, but of the state. And the president of the country, as we know, stands for the state. He is the highest state figure of authority. That's why, in most states, the national health care policy is developed under the supervision of the president. He personally coordinates the programs in that field. He has a brain trust of independent experts, and there is a national institute of health.

The "White Paper" of Russia will come out annually from here on out. The report is displayed by the president's administration. The temporary group of specialists working on it can be considered a prototype of the brain trust or the national institute. Perhaps it would make sense to commission it other research. Like research on ways to develop the pharmaceutical industry of Russia, for example. Next year, the industry is only expected to take on shareholders. There's still some time left before privatization.

### Medicines 'Unaffordable'

937C0179D Moscow KOMSOMOLSKAYA PRAVDA  
in Russian 3 Dec 92 p 13

[Article by M. Guseva: "The Pharmacy, the Dollar, and the Lantern: We Continue the Topic of Why Drugs Are, As Before, Inaccessible"]

[Text] Today, when you stop by the nearest pharmacy on the way home, you will be entering a municipal facility. Don't let the new word scare you. You can still get analgin here, as you could before. But something has, indeed, changed. So what is it?

First of all, let us reassure you by saying that the pharmacies are still owned by the state. But they've become legal entities, with all that goes with that: current accounts, balance sheets, legal addresses, etc. And that means that they have complete economic freedom now: they can buy goods where and how they please, continuing at the same time some pharmacological control. It's beneficial to the pharmacies. What speaks for itself is

that 370 of the 431 Moscow pharmacies today are already municipal, and the rest are filling out the necessary paperwork to gain that status. Is that beneficial to us, the buyers who are suffering and in pain?

In the Moscow City Pharmacy Chamber, we were assured that basically, yes, it is beneficial to us. Because in the final analysis, that economic freedom leads to a saturation of the drug market. And in fact, as soon as the pharmacists began to have their own money, their response to all the fluctuations in supply and demand was much more prompt, and there was even some additional economic activity. Not at the warehouses—the pharmacists are going to the wholesale base and concluding agreements with a middleman firm or with the producers directly. Please, treat yourselves to your heart's content!

Drop by the pharmacy trade hall today and feast your eyes on the pharmaceutical abundance. A year ago, we could have only dreamed about such an abundance! But, alas, the consumer is again dissatisfied. As in the old days, a common day-to-day truth comes to the surface: "We have everything, but when you need something specific, it's not there!" The pharmaceutical abundance is largely illusory. Things are not good, for example, with oncological and psychotropic preparations or with certain kinds of cardiovascular preparations. Even such "simple" preparations like allochol [allokhol] and activated carbon are in short supply. And at times, all we can do is just look at the drugs that are for sale. Can't buy them—they're too expensive. Take, for example, a package of trichopol [trikhopol], which was in short supply quite recently. It's available now, but for 500 rubles [R].

Does that mean that the changeover to municipal pharmacies is not a blessing in every regard? Of course. First of all, you have the prices. Today, pharmacological producers and sellers negotiate with each other on prices, in each and every case. Consequently, prices are free-floating. Then a 25-percent trade markup is added to the price, to cover the expenses associated with transport and trade and to develop sales. (By the way, today, that markup percentage is already inadequate, and it may have to be raised.) That's how prices from a certain type of which one can become ill are generated.

Even sadder is the situation with imported goods. Before, deliveries of imported goods were made to the pharmacy system through Farmimeks. When the buyers paid, the dollar was converted to rubles not at the market exchange rate, but at a special exchange rate. That system remains to this day, and there are contracts and requests, but... The Ministry of Health of the Russian Federation has a minimum of hard currency today, and as a result, the wholesale bases are empty. And the municipal pharmacies don't have their preferential quotas of hard currency. They can, of course, purchase drugs wholesale, but at market exchange rates. So it turns out that a drug that costs \$1 and that could have been purchased through a central apparatus for R90 is bought

on the market for R450. Then there's the markup. (Remember the R500 trichopol?) So what you hear more and more often in the pharmacy is this: "Isn't there a domestic substitute?"

In most cases, there is. And often, it's not even expensive. There is a list of drugs (nearly 270) whose prices are fixed. But the pharmacies take those preparations begrudgingly. Bifidus bacterin [bifidum-bakterin] is bought from the producers for R9.60 and, according to the price set on the list, must be sold for 35 kopecks, and the pharmacy is later paid the difference. But only after the product is sold, and then payment doesn't come until the end of the quarter. Is that suitable for an organization that has its own current account? The question is rhetorical. After all, the prosperity of the municipal pharmacy is a direct function of the turnover of monetary assets. To put it more succinctly, if there's money, there will be goods!

Will the municipal pharmacies be the first step on the path of their privatization? The people in that same Moscow City Pharmacy Chamber don't discount that prospect. But they don't see anything criminal in that. Both leased and private forms of ownership are possible. It's another matter that the private pharmacy today simply can't survive. The competition of semistate structures would hammer it down. But in order to get together a little faster on the road to the market, we must, as always, quickly set some boundaries first. This time, concerning the poor and the rich. Because a poor man's wallet has trouble handling not only the private pharmacy, but also the municipal pharmacy. And everyone, alas, gets sick at one point or other.

The pharmacies that for now are being called "social pharmacies" by the developers of the program will be able to protect the interests of the strata of the population that have little. Around 50 such pharmacies are planned for Moscow. From warehouses they will get commodities already subsidized, and they will get imported drugs on the basis of a special exchange rate for conversion of the dollar. As a result, prices at the counter will be acceptable both to the purchasers and for the budget. Of course, not just anyone will be able to be a customer at such a "privileged" pharmacy. The people who use the pharmacy will be those who present special prescriptions: for breast-fed children, the disabled, parents with large families, Afghanistan vets, and Chernobyl victims.

And the rich, who, as we now know, also pay, will be able to take care of their own health in the private pharmacy. And then, at least when it comes to illness, the poor and the rich will finally become equal.

### Black Market for Medicines

937C0179E Moscow KOMSOMOLSKAYA PRAVDA  
in Russian 1 Dec 92 p 2

[Article by Ye. Dotsuk, Yu. Kulibaba, V. Terekhina, and O. Chegodayeva, under the rubric "A KOMSOMOLSKAYA PRAVDA Investigation": "To Where Have All

the Drugs From Our Pharmacies Disappeared?"; first two paragraphs are source introduction]

[Text] Drugs and the market. A thing of the past, like many other things, is the notion that that's exclusively the realm of the state: to buy, produce, and sell medicinal agents. Why, who isn't buying or selling drugs today! They're being offered in commercial kiosks, from automobiles, and even from beneath the floor. And it's all kinds of things—sometimes very strong-acting drugs, other times narcotics, drugs that in the past were very hard to come by.

Alas, it's clear that drugs, as with consumer goods, are increasingly becoming for many not so much a means of helping a sick person as they are a profitable way of making money. The market is the market?

"Where did you get it?" "I bought it."

Not even a year has passed since drug prices in Russia were uncapped. With the exception, of course, of the list of 270 preparations that are needed primarily by the seriously ill and the poor. They say that if you're lucky, you can still buy aspirin in a pharmacy for 20 kopecks (!) a package. But...

As they said at 38 Petrovka, one big roundup made recently by the Moscow police at the markets resulted in the arrest of 39 people—private sellers of scarce drugs. The reason for the arrests was the presidential edict "Free Trade," which, as we know, forbids the sale of drugs by individuals (and that goes for weapons and narcotics, too). To the question of where they got the drugs, all of them give the same answer—"We bought them"—although, presumably, they don't produce any prescriptions. In the meantime, the newspapers are increasingly filled with ads that read "Private individual (P.O. box whatever) offers unlimited quantities of..." Just how are drugs today getting into the hands of these anonymous private individuals?

**Deputy chairman of the state concern Farminindustriya, Yu. Yenyutin:**

"After the ceiling was removed from prices, producers ran into a problem with sales. Our production capacities are large enough to supply drugs to Russia and the countries around us, but... With the money shortage, our buyers—Rosfarmatsiya and its regional associations—don't have enough money to buy the expensive drugs. And they weren't able to get loans.

"Things are very bad with the drugs that have gotten on the above-mentioned privileged list. Those drugs are are drugs that are the most badly needed, but the pharmacies are generally not interested in selling them.

"As a result, the producers have been forced to restrain production, the wholesalers are tied up in loans, and the pharmacies, to survive, are selling drugs to those who can pay.

"The private drug business today is flourishing. There is, of course, a trading house Lekarstva Rossii [Drugs of

Russia] in Moscow, which exists under the concern Farminindustriya and sells drugs through commercial structures, and there are similar firms in Siberia, but they are operating for now with very small volumes, and the firms aren't solidly on their feet yet. And there's no doubt that the drugs getting into the hands of private sellers represents a dangerous trend. After all, none of them can keep track of the conditions associated with storage or transport—never mind how much harm the unregulated sale of strong-acting agents could do. Licensing needs to be introduced for the sale of drugs, and the sooner the better."

### And Here's an Aspirin for You, Grandma

In Ukraine, it's easier to die immediately than to live a long time on tablets. After seeing a package of no-shpa for 768 coupons in one of the pharmacies, an elderly lady who earned a state pension that would cover only 20 tablets fainted. As they say, they've barely just come out.

In the near future, in Dnepropetrovsk, yet another "cheap" item, one bought in the United States, will appear. It's aspirin, without which it would be very difficult to fight colds in the winter. One tablet costs 15 coupons, but the scarce items were acquired for medical institutions, and you won't find them in the pharmacies. What price they'll be on the black market, God only knows.

### We'll Assault the Shortage With Prices

The rumors about the coming colossal rise in drugs prices, it would seem, have been confirmed. The Cabinet of Ministers of Kazakhstan adopted a special decree after establishing in November free-floating prices for all types of medicinal agents and for other medical-related articles, except those that are imported.

Before that, the drug situation was truly paradoxical: The drugs would be bought by Kazakhstan at unreasonably high wholesale prices and sold in the republic at extremely low retail prices. The retail price, for example, might be 50 times lower than the wholesale price. With figures like that, by the way, one can understand how much prices have jumped now.

Attached to the decree, in fact, is a list of those social groups of the populace that will be able to get drugs free-of-charge or at huge discounts, but only by prescription.

### New Requirements for Pharmacists

937C0179F Moscow ROSSIYSKIYE VESTI in Russian  
14 Nov 92 p 2

[Article by Oksana Dul'skaya, under the rubric "Protect Yourself!": "If a Drug Is Not Available in a Pharmacy, Here's a Prescription for the Readers of ROSSIYSKIYE VESTI"; first paragraph is excerpt from letter by Ye. Latygina, of Moscow]



[Text] "It's no secret to anyone that the country right now is in bad straits when it comes to drugs. A physician writes a prescription, but they show you the door in the pharmacy. It's virtually impossible to find out why this or that drug is not available, and the answer is always that same: 'It didn't come in.'"

But a lot depends on the pharmacy worker in this situation. There exists RSFSR Ministry of Health order No. 463 dated 6 Aug 1980, which has not been abolished by anyone: "Confirmation of the Time Regulations for the Operation of the Cost-Accounting Pharmacy in Terms of Serving the Public." Point 6 of that order says the following. When a prescription for a drug that is not available for sale at a given moment comes into a pharmacy, the administration must get in touch with the physician about a substitution if the pharmacy expects that the drug will not come in for a long time. If there is a possibility that the preparation can be obtained from the warehouse, then the prescription is left in the pharmacy "for further support," and the administration must report promptly to the patient when the needed drug appears.

#### **Sharp Rise in Birth Defects in Mogilev Oblast**

937C0179G Moscow NEZAVISIMAYA GAZETA  
in Russian 29 Aug 92 p 6

[Article picked up from the Russian Information Agency wire service: "Deformed Babies Are Being Born More and More Often"]

[Text] The Mogilev Oblast Medical Genetics Center in the first half of this year recommended that pregnancy be terminated in 34 women in order to avoid the danger of their giving birth to babies with congenital pathology. Over all of last year, there were only 48 such recommendations.

#### **Kazakhstan Frees Pharmaceutical Prices, Guarantees Free Medicines to Population Subgroups**

937C0179H Alma-Ata KAZAKHSTANSKAYA  
PRAVDA in Russian 20 Nov 92 pp 1, 2

[Article from KazTAG service: "Drugs Prices Freed. It Will Be Hard To Get Treated. But Privileges Are Provided: Who Will Get Medications for Free or for Reduced Prices"]

[Text] There's been a lot of talk lately about the indiscriminate rise in drug prices in the republic. So what about it?

Yes, to saturate the market and prevent the drain-off of drugs and medical items to places outside the republic, the Cabinet of Ministers has adopted a special decree.

The decree established free-floating retail prices for all types of drugs and medical items, except those that are imported, beginning 16 November of this year, with a

partial amendment of point 2 of the 3 January 1992 government decree, "Measures to Liberalize Prices," and of its Appendix 2.

The action of point 2 of the Cabinet of Ministers 2 September 1992 decree, "The Size of the Trade Markups and the Maximum Levels of Profitability for Trade Organizations and Supply-and-Sales Organizations," has been extended to enterprises and organizations of the Farmatsiya Production Association.

In outpatient treatment based on physician-written prescriptions, medications are released free of charge or with privileges on the basis of an approved list of population groups and disease categories.

The Ministry of Health has been commissioned with releasing drugs via special physician-written prescriptions to the populace on a privileged basis through pharmacy institutions, with collection of some of the cost. The prescriptions are written in one copy and remain in the pharmacy institution for further submission to treatment-prevention institutions for payment.

**List of population groups and disease categories in the outpatient treatment of which medications are released free of charge to the patients via physician-written prescription**

##### **I. Population groups:**

- Great Patriotic War disabled persons and other similarly disabled persons;
- children 16 or under who have been disabled since early childhood;
- children 3 years old or under;
- veterans of the Great Patriotic War, as well as the parents and wives of military servicemen who died as a result of wounds, contusions, or mutilations suffered in defense of the USSR or while performing other military duties or as a result of disease associated with being on the front;
- citizens who are former internationalist/military servicemen who took part in the military actions in Afghanistan or other countries;
- former prisoners of fascist concentration camps who were minors (16 or under when liberated);
- children who were victims of the accident at the Chernobyl Nuclear Power Plant;
- pregnant women who lived in areas affected by the accident at the Chernobyl Nuclear Power Plant;
- individuals with radiation sickness resulting from the accident at the Chernobyl Nuclear Power Plant or from performing cleanup operations, when a causal effect is established between the disability and the accident or the performance of the cleanup operations;
- family members of citizens who were killed or who later died as a result of the accident at the Chernobyl Nuclear Power Plant or the cleanup.



## II. Disease categories:

- oncological and hematological;
- diabetes mellitus, and other forms of diabetes;
- rheumatism (bicillin for antirelapse therapy);
- postsurgical conditions following operations involving heart valves prostheses (anticoagulants);
- acute intermittent porphyria (adenyl, domestic fosfaden);
- severe form of brucellosis (antibiotics);
- mental illnesses (group I and II disabled and individuals working in medical production shops of psychiatric and psychoneurological institutions);
- pemphigus and systemic (acute) lupus erythematosus;
- systemic, chronic, severe diseases of the skin;
- syphilis;
- leprosy;
- tuberculosis;
- Addison's disease;
- schizophrenia and epilepsy;
- hepatocerebral dystrophy and phenylketonuria;
- mucoviscidosis (ill children);
- bronchial asthma (ill children);
- dysentery;
- hypophyseal nanism;
- postsurgical condition following kidney transplant;
- Bekhterev's disease;
- Parkinson's disease;
- myasthenia;
- myopathy;
- Marie's ataxia;
- infantile cerebral paralysis;
- premature sexual development;
- AIDS, HIV-infected individuals;
- postsurgical condition following heart or liver transplant;
- myocardial infarction (first six months).

NOTE: In accordance with the Kazakh SSR law "Local Self-Government and Local Soviets of People's Deputies of the Kazakh SSR," the heads of oblast and Alma-Ata and Leninsk city administrations are given the right to insert additions to this list.

**List of populations groups in the outpatient treatment of whom drugs prescribed by physicians are released at special prices**

### I. At 50 percent of cost:

- citizens who worked during the siege of Leningrad at city enterprises and who were awarded the Defense of Leningrad medal;
- people in disability group I or II as a result of a work injury or an occupational or general disease;
- group I and II individuals disabled since childhood and receiving assistance;
- retirees from the military and from among workers, office workers, and kolkhoz workers receiving the smallest pension for age or disability or for loss of a breadwinner;

- retirees awarded orders or medals of the USSR for selfless work or exceptional military service in the rear or during the Great Patriotic War;
- citizens awarded the Resident of Besieged Leningrad badge of the ispolkom of the Leningrad City Soviet of People's Deputies;
- individuals who took part in the 1986-1987 cleanup operations for the accident at Chernobyl;
- family members of military personnel, individuals of leadership and line positions called to military duty, workers and office workers of the USSR Ministry of Defense, the USSR Ministry of Internal Affairs, and the USSR Committee for State Security who were killed or who died during the performance of assignments associated with the protection of social order in emergency circumstances associated with antisocial phenomena;
- citizens who were unjustly brought to trial and who were subjected to other judicial and extrajudicial repressions for sociopolitical reasons in the 1930's, 1940's, and early 1950's; who were pronounced disabled as a result of illness in places where they were deprived of their freedom (with the exception of individuals whose disability resulted from illegal activities or general illness after being set free); and individuals who are widows of citizens rehabilitated posthumously and who have not remarried.

### II. Payment of 20 percent of the cost:

- retirees on individual pensions and the members of their family who are dependent on them.

NOTE: In accordance with the Kazakh SSR law "Local Self-Government and Local Soviets of People's Deputies of the Kazakh SSR," the heads of oblast and Alma-Ata and Leninsk city administrations are given the right to insert additions to these lists.

## Joint Ventures of Sechenov Academy

937C0184A Moscow MOSCOW NEWS in English  
No 31, 2-9 Aug 92 p 9

[Interview of Mikhail Paltsev, rector of Moscow Sechenov Medical Academy, by Maria Temchina: "Looking for a Way Out"]

[Text] An MN correspondent talks to Mikhail Paltsev, rector of Moscow Sechenov Medical Academy, on the situation in medical research and the problems facing the country's most prestigious medical research centre.

[Temchina]: Now that budget allocations for research have been so drastically reduced, how do you in the academy manage to carry on with your work?

[Paltsev]: Were it not for the academy's commercial structures, we would have had to halt research altogether. We just don't have any other source of money to modernize our clinics and laboratories and do repairs of buildings and dormitories.

Take, for instance, a Russian-Singaporean joint venture, Quorum, which made it possible to start the industrial production of heart valves, artificial vessels and skin for transplants, and an effective yet inexpensive collagen-based preparation, all of which have been designed by our researchers. One other joint venture, Pharma-Eks, helped us manufacture mammal implants now widely used in Moscow hospital No. 61 with wonderful results.

But there is one other thing. a dramatic rise in prices left the practitioners and researchers in a complete information vacuum. Because of a lack of money, we can't subscribe to foreign medical journals. We hardly have the means to cover domestic trips. Now, thanks to the profit we get from joint ventures, we can finance our experts' trips to international conferences, which is

practically the only opportunity for us to learn the latest achievements in medical research.

**[Temchina]:** Now you can have one more source of income—paid medical service.

**[Paltsev]:** Hardly. In my view any person, particularly with health problems, should have the right to choose. What contributed to the glory of Moscow's 1st Medical Institute is its personnel's professionalism and traditions, one of which was free and available medical treatment. In its hospital wards, you could meet patients from different walks of life and different incomes. That was an achievement we were always proud of. As for the paid services, we don't say "no" to them. In fact, there is a joint-stock company, Sodeistviye, headed by Professor Kuzin, that has been formed under the academy to provide paid treatment.

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